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EXAMINER	
REDDIG, PETER J	

ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/810,751	YOUNG ET AL.	
	Examiner	Art Unit	
	Peter J. Reddig	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *6-10,17-21 and 29-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,11-16 and 22-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/28/05; 6/30/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The Election filed October 13, 2006 in response to the Office Action of September 14, 2006 is acknowledged and has been entered.

Applicant's election with traverse of Group I, claims 1-28 and the species (A2) non-conjugated antibodies, (C1) antibody -dependent cellular cytotoxicity, (D1) colon, and species (E1) murine is acknowledged.

2. Applicants argue that claims 33-40 do not recite the phrase "selected from the group consisting of . . ." and thus are not presented in a Markush format.

This argument has been considered but has not been found persuasive because MPEP 803.02 specifically states that "A Markush-type claim recites alternatives in a format such as "selected from the group consisting of A, B and C." It is clear that it is not required that the language "selected from the group consisting of" be used. In particular, claim 33 from which claims 34-40 depend specifically recites the phrase "and/or" thus the claim limitations are clearly recited in the alternative and meets the limitations of the Markush format, see also MPEP 2173.05(h)(ii) which specifically states that the language "or" is acceptable Markush language.

3. Applicants argue that the inventions of Groups I, III and IV have the same objectives, method steps and criteria for success. Applicants argue that Group I is drawn to a method of treating a patient suffering from a cancerous disease by administering a monoclonal antibody encoded by a clone deposited with the ATCC as PTA-4890. Applicants argue that Group III is drawn to a method of extending survival by treating a human tumor, i.e. cancerous disease, by administering a monoclonal antibody encoded by a clone deposited with the ATCC as PTA-4890. Applicants argue that Group IV is drawn to a method of delaying disease progression by

treating a human tumor, i.e. cancerous disease, by administering a monoclonal antibody encoded by a clone deposited with the ATCC as PTA-4890. Applicants argue that thus, it is clear that the three groups have the same objective, i.e. treatment of cancerous disease, carried out by the same method, i.e. administration of a monoclonal antibody encoded by a clone deposited with the ATCC as PTA-4890.

Applicants argue that the treatment methods of Groups I, III and IV and the binding assay of Group II are each dependent upon the ability of the monoclonal antibody to interact with a CD63 antigenic moiety. Applicants argue that thus, Groups I-IV have the same criteria for success, i.e. the binding of the monoclonal antibody to a CD63 antigenic moiety.

Applicants' arguments have been carefully considered and are found persuasive, in part. Groups III and IV will be rejoined because extending survival and delaying disease progression are overlapping criteria for success because delaying disease progression would be expected to extend survival.

However, Groups I and Groups III/IV will remain separated for the reasons of record and the following reasons. Although applicants argue that Groups I and Groups III/IV have the same objective and method, the objective of Group III/IV is distinct from that of Group I in that Group III/IV is a method that requires extending survival and/or delaying disease progression and Group I does not. Additionally, Group I requires that the antibody of the method be characterized as being cytotoxic against cells of a cancerous tissue and Group III/IV does not have this limitation. Thus different searches and issues are involved in the examination of each Group and the literature search, particularly relevant in this art, is not coextensive.

Applicants argue that Group II and Groups I and III/IV are dependent on the ability of the monoclonal antibody to interact with a CD63 antigenic moiety. However, the success of the treatment methods of Groups I and III/IV depend not only on the antibody binding to its target antigen, but also on a host of other in vivo factors such as CD63 availability, the prevalence of CD63 on the target tissue, and non-specific binding of the antibody to other targets in vivo. Thus different searches and issues are involved in the examination of each Group and the literature search, particularly relevant in this art, is not coextensive. Additionally, because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions have acquired a separate status in the art in view of their different classification, restriction for examination purposes as indicated is proper

4. Applicants argue that the non-conjugated and conjugated antibodies are not independent inventions since conjugation is a further limitation on the antibody. Applicants argue conjugated antibodies comprise the same antibody as the non-conjugated antibodies (shared structure), which work by binding a CD63 antigenic moiety (shared mode of operation) to treat a cancerous disease (shared effects). Applicants argue a search for a non-conjugated antibody and the conjugated antibody clearly overlaps.

Upon review and reconsideration, given that the conjugation of antibodies to cytotoxicity enhancing compounds for enhanced efficacy in cancer treatment is well known in the art, the requirement for the election of species between an unconjugated and conjugated antibody will be vacated.

5. Applicants argue that the types of conjugates (toxins, enzymes, radioactive compounds and hematogenous cells) are presented in a Markush format. Applicants argue that the restriction of a Markush group is proper only where the compounds within the group either (1) do not share a common utility, or (2) do not share a substantial structural feature disclosed as being essential to that utility.

Applicants argue that the four types of conjugates disclosed share both a common utility, i.e. treatment of a cancerous disease, and a common structural feature, i.e. each type is conjugated with the specific monoclonal antibody encoded by the clone deposited with the ATCC as PTA-4890. Applicants argue that utility of the treatment is dependent upon the binding of the monoclonal antibody to a CD63 antigenic moiety, i.e. the four types of conjugates share an antibody, which is essential to the utility as disclosed (treatment of cancerous disease). Applicants argue that a search for each of the four types of conjugates clearly overlaps.

This argument has been carefully considered, but has not been found persuasive. The members of the Markush Group do not share a structural feature that is essential to their utility. The antibody is not a structural feature of each member of this group. The utility of these conjugates is in their toxicity and the structurally required features for this utility are clearly distinct for toxins, enzymes, radioactive compounds and hematogenous cells. Additionally different searches and issues are involved in the examination of each conjugate and the literature search is not coextensive. Thus, the restriction of the Markush group is deemed proper.

However, the Markush group of conjugates will be rejoined given that conjugated and unconjugated antibodies have been rejoined for examination and in the interest of facilitating prosecution.

7. Applicants argue that all six types of cytotoxicity mediated by the described antibody are not independent inventions because each type places a further limitation on the antibody by defining how the cytotoxicity of the antibody is achieved. Applicants argue that all six types have the same effect, i.e. cytotoxicity. Applicants argue that a search of the prior art should center on the specific monoclonal antibody. Applicants argue that one of skill in the art would not attempt to search each of the six types of cytotoxicity mediated without connecting the search to the antibody since a search of the six types alone would result with thousands of hits related to many different antibodies. Applicants argue that the search for types of cytotoxicity is considered overlapping and thus, the election of species is improper.

Applicants' argument has been considered, but has not been found persuasive because, for example, different antibody isotypes differ in their ability to stimulate complement-mediated cytotoxicity or antibody dependent cellular mediated cytotoxicity. Additionally, one of ordinary skill in the are would not predict that all antibodies, even those directed to the same antigen, would mediate all of the mechanisms of cytotoxicity claimed. For example not all antibodies have catalytic activity or can interfere with the function of the antigen they bind. Thus, the antibodies that effectively mediate each of theses forms of cytotoxicity are distinct and thus the literature search is not coextensive. Thus different searches and issues are involved in the examination of each species.

Applicant argues that each type of tumor tissue is not an independent or distinct invention. Applicant argues that the tumor tissue is not a step of the described methods. Applicants argue that cells obtained from all of these tumor tissues were used with the same claimed methods. Applicants argue that these methods operate the same way in all of the tissues,

i.e. the antibody binds a CD63 antigenic moiety in all of the tissues. Applicants argue that the instant inventors found that human tumor cells obtained from colon, ovarian, lung, prostate, and breast tissues expressed a CD63 antigenic moiety on their surfaces and thus were able to be treated successfully with the described monoclonal antibody encoded by the clone deposited with the ATCC as PTA-4890. Applicants argue that a search of the prior art regarding tumor tissues should center on the specific monoclonal antibody and the search for types of tumor tissue is considered overlapping and thus, the election of species is improper.

Although the methods of treating different cancers with PTA-4890 are distinct, upon review and reconsideration and in view of the effectiveness of the antibody in treating breast and prostate tumors, the species election for tissue of tumor is vacated and the species will be will be rejoined for examination.

8. Applicants argue that that there are no human antibodies disclosed; the antibodies disclosed in the instant specification are murine antibodies and murine antibodies that have been humanized.

Upon review and reconsideration, the election of species between human and murine antibodies will be vacated.

The issues remain the same for the reasons set forth previously and above, thus the restriction requirement is deemed to be proper and is therefore made FINAL.

9. Claims 1-40 are pending.

10. Claims 6-10, 17-21, and 29-40 are hereby withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to a non-elected invention.

11. Claims 1-5, 11-16, and 22-28 are currently under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1-5, 11, and 23-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-5, 11, and 23-28 are indefinite because claims 1 and 23 recite the phrase "identifying characteristics". The claims are indefinite because the specification provides no definition of "identifying characteristics". Thus it is not possible to determine if the identifying characteristics of the claimed product used in the claimed method are drawn to the product's characteristics as a monoclonal antibody, as a protein, as a binder to a particular antigen, or as a binder to a cancer cell. Given the above, the metes and bounds of the subject matter claimed cannot be determined and neither the specification nor the claims as originally filed particularly points out or distinctly claims the subject matter which applicant regards as the invention.

13. Claims 1-5 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-5 and 11 are indefinite because claim 1 is drawn to administering an anti-cancer antibody or fragment thereof, which encompasses the Fc and antigen binding fragments, and is also drawn to said antibody being an isolated monoclonal antibody or antigen binding fragment thereof. It is unclear if the claims are encompassing both antibody fragments which bind to a

target antigen, i.e. the antigen binding fragments, and fragments that would not bind to the target antigen, i.e. the Fc region of the antibody. Thus, the metes and bounds of the claim cannot be determined.

14. Claims 2, 4, 13, 15, 24, and 26 are indefinite because it recites the phrase a "chimerized antibody". The exact meaning of the word chimera is not known. The term chimera is generic to a class of antibodies which are products of genetic shuffling of antibody domains and other active proteins. The term encompasses antibodies fused to non-immunoglobulin proteins as well as antibodies wherein any domain of the antibody is substituted by corresponding regions or residues of human antibodies including but not limited to CDR grafted antibodies. Thus the metes and bounds of the claim protection sought cannot be determined.

15. Claims 1-5, 11-16, and 22 are indefinite because claims 1 and 12 recite the phrase "essentially benign". The claims are indefinite because the specification provides no definition of "essentially benign". Thus it is not possible to determine what essentially benign is. For example, does essentially benign mean that the antibody is benign to a certain percentage of non-cancerous cells? If so, what percentage? Does essentially benign mean that the antibody affects all non-cancerous equally in some less than toxic manner? Given the above, the metes and bounds of the subject matter claimed cannot be determined and neither the specification nor the claims as originally filed particularly points out or distinctly claims the subject matter which applicant regards as the invention.

16. Claim 15 recites the limitation "said subset". There is insufficient antecedent basis for this limitation in claim 14 from which claim 15 depends.

17. Claim 28 recites the limitation "humor tumor tissue sample" in claim 23. There is insufficient antecedent basis for this limitation in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

18. Claims 23-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re* Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. See also *Ex parte* Forman, 230 USPQ 546 (BPAI 1986).

The claims are drawn to a process for mediating cytotoxicity of a human tumor cell which expresses a CD63 antigenic moiety on the cell surface comprising: contacting said tumor cell with an isolated monoclonal antibody or antigen binding fragment thereof, said antibody or antigen binding fragment thereof being an isolated monoclonal antibody or antigen binding fragment thereof which binds to said expressed CD63 antigenic moiety, said antigenic moiety characterized as being bound by an antibody having the identifying characteristics of a monoclonal antibody encoded by the clone deposited with the ATCC as PTA-4890, whereby cell cytotoxicity occurs as a result of said binding.

The monoclonal antibody encoded by the clone deposited with the ATCC as PTA-4890, also referred to in the specification as 7BD-33-11A, will be referred to as PTA-4890.

The specification teaches, based on mass spectroscopic identification combined with the confirmatory immunoprecipitation, western blotting experiments using known CD63 antibodies, and testing the reactivity of PTA-4890 against different isolated extracellular domains of CD63, that the antigen for PTA-4890 is CD-63 and PTA-4890 binds the extracellular region of CD63 encompassing amino acids 108-202, see p. 40, lines 21-23, Example 2, and Fig. 4-9

The specification teaches that PTA-4890 was specifically cytotoxic in breast and prostate tumor cell lines selectively, and did not affect normal cells in *in vitro* assays, see p. 42, lines 20-22 and Table 1. The specification teaches that PTA-4890 had cytotoxic activity against the breast cancer cell lines MCF-7 and PC-3 prostate cancer cell line, but not the MDA-MB-468, MDA-MB-231, HT-29, SW116, SW620, NCI H460 tumor cell lines, see Table 1.

The specification teaches that PTA-4890 displayed specific tumor binding to the MCF-7, PC-3, MDA-MB-468, MDA-MB-231, HT-29, SW116, SW620, and NCI H460 tumor cell lines

and other tumor cell lines, see Table 2. The specification teaches that there was also binding of PTA-4890 to non-cancer cells, however that binding did not produce cytotoxicity. The specification teaches that this was further evidence that binding was not necessarily predictive of the outcome of antibody ligation of its cognate antigen, and was a non-obvious finding. The specification teaches that this suggested that the context of antibody ligation in different cells was determinative of cytotoxicity rather than just antibody binding, see para. bridging p. 44 and 45.

One cannot extrapolate the teachings of the specification to the enablement of the claims because no nexus has been established between contacting a cell with PTA-4890, the expression of CD63, and the induction of cell cytotoxicity as a result of the binding PTA-4890. The specification teaches that in the 7 tumor lines for which there is corresponding binding and toxicity data, only in 2 of the cell lines, MCF-7 and PC-3, does the binding of CD63 by PTA-4890 positively correlate with cytotoxicity. Thus, in only 29% of the tumor cells does the binding of PTA-4890 positively correlate with the induction of cytotoxicity or, restated, in 71% of the cells that PTA-4890 bound no cytotoxicity was observed.

Thus, the given the above, one of ordinary skill in the art could not reasonably predictably identify an antibody that binds to CD63 that has the identifying characteristics of PTA-4890, that is an antibody that would bind to and have cytotoxicity on two cell lines but not on 5 others,with a reasonable expectation of success without undue experimentation.

Applicant is reminded that MPEP 2164.03 teaches "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 428 F.2d 833, 166 USPQ 18, 24 (CCPA

1970) the amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly state in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order for it to be enabling. Given only lack of guidance in the specification, no one skilled in the art would accept the assertion that the claimed invention would function as contemplated or as claimed based only on the information in the specification and that known in the art at the time the invention was made.

The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the invention will function as claimed with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

17. If applicants were able to overcome the rejections set forth above claims 1-5, 11-16, and 22-28 would still be rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating a patient suffering from **breast or prostate cancer** or for mediating cytotoxicity of **a breast or prostate tumor cell** with a monoclonal antibody encoded by the cloned deposited with the ATCC as PTA-4890, does not reasonably provide enablement for a method for treating a patient suffering from **a cancerous disease** or for

mediating cytotoxicity of **a human tumor cell** with a monoclonal antibody encoded by the cloned deposited with the ATCC as PTA-4890. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to a method for treating a patient suffering from **a cancerous disease** or for mediating cytotoxicity of **a human tumor cell** with PTA-4890.

This means that one can treat a patient suffering from **any** cancerous disease or mediate cytotoxicity in **any** human tumor cells with PTA-4890.

The specification teaches that the breast cancer cell line MCF-7 and prostate cancer cell line PC-3 were susceptible to the cytotoxic effects of PTA-4890 in vitro. The specification teaches that the result of PTA-4890 cytotoxicity against breast and prostate cancer cells in culture was further extended by its anti-tumor activity towards these cancer indications in vivo (as disclosed in Ser. No. 10/348,231 and Ser. No. 10/603,006), see p. 14, lines 14-18.

The specification teaches that PTA-4890 treatment, at 3 different doses, significantly reduced tumor burden and increased survival in comparison to an isotype control antibody in i*n vivo* MDA-MB-231 preventative dose response tumor experiments. The specification teaches that treatment at the highest dose with PTA-4890 demonstrated the greatest reduction in tumor growth (100 percent) and the largest increase in survival (all mice are still alive), see Example 7 and Figs. 15 and 16.

One cannot extrapolate the teaching of the specification to the scope of the claims because the art teaches that PTA480 is selective for breast and prostate cancer cells in its

cytotoxic activity and the heterogeneity of cancers and their response to treatment is well known in the art.

1) In particular, as drawn to the heterogeneity of cancers, Young et al. (US Pat. No. 7,009,040 B2, 2003) teach that PTA-4890 (7BD-33-11A) was specifically cytotoxic in breast and prostate cancer cells, see column10 and Table 2. Furthermore, Young et al. teach that the antibodies were selective in their activity since not all cancer cell types were susceptible, see columns 10 and 11.

Furthermore, the art teaches that cancers comprise a broad group of malignant neoplasms divided into two categories, carcinoma and sarcoma. The carcinomas originate in epithelial tissues while sarcomas develop from connective tissues, see Taber's Cyclopedic Medical Dictionary (1985, F.A. Davis Company, Philadelphia, p. 274). Given that not all cancers originate from the same tissue types, it is expected and known that cancers originate from different tissue types have different structures as well as etiologies and would present differently. Thus, it would not be predictably expected that a nexus, for example drawn to a connection between PTA-4890 and treating a patient suffering from a cancerous disease, would be established between two cancer types that arose from different tissue types. Further, it is well known that even two carcinomas that present on the same organ have significant differences in etiology and genetic constitution. For example, Busken, C et al, (Digestive Disease Week Abstracts and Itinerary Planner, 2003, abstract No: 850), teach that there is a difference in COX-2 expression with respect to intensity, homogeneity, localization and prognostic significance between adenocarcinoma of the cardia and distal esophagus, suggesting that these two cancers have different etiology and genetic constitution (last five lines of the abstract). Furthermore

Krontiris and Capizzi (Internal Medicine, 4th Edition, Editor-in-chief Jay Stein, Elsevier Science, 1994 Chapters 71-72, pages 699-729) teach that the various types of cancers have different causative agents, involve different cellular mechanisms, and, consequently, differ in treatment protocols. Chemotherapeutic agents are frequently useful against a specific type of neoplasm and especially with the unpredictability of the art there are no drugs broadly effective against all forms of cancer, see Carter, S. K. et al. Chemotherapy of Cancer; Second edition; John Wiley & Sons: New York, 1981; appendix C. Given the above, it is clear that it is not possible to predictably extrapolate a correlation between PTA-4890 and treating a patient suffering from a cancerous disease or mediating cytotoxicity of a human tumor cell in any tumor type other than breast and prostate cancer, based on the information in the specification and known in the art without undue experimentation.

Applicant is reminded that MPEP 2164.03 teaches "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 428 F.2d 833, 166 USPQ 18, 24 (CCPA 1970) the amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly state in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order for it to be enabling. Given only lack of guidance in the specification, no one skilled in the art would accept the assertion that the claimed invention would function as

contemplated or as claimed based only on the information in the specification and that known in the art at the time the invention was made.

The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the invention will function as claimed with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

18. If applicants were able to overcome the rejections set forth above under 35 U.S.C. 112, claims 1-5, 11 and 23-28 would still be rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating a patient suffering from a cancerous disease or for a process for mediating cytotoxicity with a monoclonal antibody or antigen binding fragment encoded by the cloned deposited with the ATCC as PTA-4890, does not reasonably provide enablement for a method for treating a patient suffering from a cancerous disease or for a process for mediating cytotoxicity of a human tumor cell with a monoclonal antibody or antigen binding fragment **having the identifying characteristics** of a monoclonal antibody encoded by the cloned deposited with the ATCC as PTA-4890. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are broadly drawn to a method for treating a patient suffering from a cancerous of a disease or for mediating cytotoxicity of a human tumor cell with a monoclonal antibody or antigen binding fragment **having the identifying characteristics** monoclonal

antibody encoded by the cloned deposited with the ATCC as PTA-4890.

This means that one can treat a patient suffering from a cancerous disease or mediate cytotoxicity in a human tumor cells **with any** monoclonal antibody or antigen binding fragment **having the identifying characteristics** monoclonal antibody encoded by the cloned deposited with the of ATCC as PTA-4890.

The specification teaches as set forth above.

Although the specification teaches that PTA-4890 binds to CD63, it does not define in the specification what the identifying characteristics of PTA-4890 are.

One cannot extrapolate the teaching of the specification to the scope of the claims because there is insufficient guidance and direction as to how to make and use antibodies which **have the identifying characteristics** of monoclonal antibody PTA-4890 because those characteristics are not defined, no antibody, other than PTA-4890, has been shown to function as claimed and it cannot be predicted that any antibody with any set of identifying characteristics of PTA-4890 will function as claimed. Further, it is well known that the art of anticancer drug discovery for cancer therapy is highly unpredictable.

In particular, Gura (Science, 1997, 278:1041-1042) teaches that researchers face the problem of sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile and teach that since formal screening began in 1955, many thousands of drugs have shown activity in either cell or animal models but that only 39 have actually been shown to be useful for chemotherapy (p. 1041, see first and second para). Because of the known unpredictability of the art in the absence of experimental evidence that any antibody (other than PTA-4890) with the undefined identifying characteristics of a monoclonal

antibody encoded by a clone deposited with the ATCC as PTA-4890 would function as claimed, no one skilled in the art would believe it more likely than not that any said antibodies are anti-cancer antibodies useful for cancer treatment or for a process of mediating cytotoxicity of a human tumor cell which expresses an CD63 antigenic moiety.

Applicant is reminded that MPEP 2164.03 teaches "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 428 F.2d 833, 166 USPQ 18, 24 (CCPA 1970) the amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly state in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order for it to be enabling. Given only lack of guidance in the specification, no one skilled in the art would accept the assertion that the claimed invention would function as contemplated or as claimed based only on the information in the specification and that known in the art at the time the invention was made.

The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the invention will function as broadly claimed with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

19. If applicants were able to overcome the rejections set forth above under 35 U.S.C. 112, claims 5 and 16 would still be rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating a patient suffering from a cancerous disease with a monoclonal antibody encoded by the cloned deposited with the ATCC as PTA-4890, wherein the cytotoxicity of said **antibody is mediated through antibody dependent cellular cytotoxicity**, does not reasonably provide enablement for a method for treating a patient suffering from a cancerous disease with a monoclonal antibody encoded by the cloned deposited with the ATCC as PTA-4890, wherein the cytotoxicity of the **antibody fragment is mediated through antibody dependent cellular cytotoxicity**. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to a method for treating a patient suffering from a cancerous disease with a monoclonal antibody encoded by the cloned deposited with the ATCC as PTA-4890, wherein the cytotoxicity of said **antibody or fragment thereof** is mediated through antibody dependent cellular cytotoxicity.

This means that **any** fragment of PTA-4890 will be effective for mediating antibody dependent cellular cytotoxicity.

The specification teaches as set forth above.

One cannot extrapolate the teachings of the specification to the scope of the claims because the specification does not teach **any** fragment of PTA-4890 for inducing antibody

dependent cellular cytotoxicity and the art teaches that antibody must retain the Fc portion of the antibody for induction of antibody mediated cellular cytotoxicity.

In particular, fragments of antibodies include not only the antigen-binding region but also the Fc portion (Roitt et al., Immunology, Fourth Edition (Mosby, London England) p. 1.6-1.7). Furthermore, it is well established in the art that antibody-dependent cellular cytotoxicity is mediated through the interaction between the Fc region of an antibody and Fc receptors present on cells of the immune system (Presta et al., Biochemical Society Transactions, 30(4):487-490, 2002). Presta et al teach that immune system recruitment can be ablated by using antigen-binding fragments such as F(ab) or F(ab)2 (see page 487, right column), as these molecules do not contain an Fc region.

Thus, one of ordinary skill in the art would not reasonably predict that any fragment of PTA-4890 would mediate antibody mediated cellular cytotoxicity without the antigen binding fragment to direct the antibody to the target cell and the Fc portion to stimulate the antibody mediated cellular cytotoxicity.

Thus, one of skill in the art could not predict that the invention would function as claimed. Therefore, practice of the invention would require undue experimentation

20. If applicants were able to overcome the rejections set forth above under 35 U.S.C. 112, claims 1-5, 11, and 13-16 would still be rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating a patient suffering from a cancerous disease with a monoclonal antibody **or antigen binding fragment** encoded by the cloned deposited with the ATCC as PTA-4890, does not reasonably provide enablement for a method for treating a patient suffering from a cancerous disease with a monoclonal antibody or

fragment thereof encoded by the cloned deposited with the ATCC as PTA-4890. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Due to the indefinite nature of claim 1, it is assumed for examination purposes that it is drawn to both antigen binding and non-antigen binding fragments, i.e. Fc fragments, of PTA-4890.

The claims are broadly drawn to a method for treating a patient suffering from a cancerous disease with a monoclonal antibody or **fragment thereof** encoded by a clone deposited with the ATCC as PTA-4890.

This means that **any** fragment of PTA-4890 will be effective for treating a patient suffering from a cancerous disease.

The specification teaches as set forth above.

The teaching of the specification cannot be reasonably extrapolated to enable the scope of the claims because one of skill in the art could not predict that any fragment of PTA-4890 would be useful for treating a patient suffering from a cancerous disease. Fragments of antibodies include not only the antigen-binding region but also the Fc portion (Roitt et al., Immunology, Third Edition (Mosby, London England) p. 1.7). One of skill in the art would expect that only antigen-binding fragments of the PTA-4890 antibody would be useful treating a patient suffering from a cancerous disease because only it would be able to bind to the target antigen. Thus, one of skill in the art could not predict that the invention would function as claimed. Therefore, practice of the invention would require undue experimentation

21. If applicant were able to overcome the above rejections set forth above under 35 U.S.C. 112, first paragraph, claims 1, 3, 5, 11, 12, 14, 16, 22, 23, 25, and 27 would still be rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating a patient suffering from a cancerous disease or for a process for mediating cytotoxicity with a monoclonal antibody encoded by the cloned deposited with the ATCC as PTA-4890, wherein said antibody is a **humanized** antibody, does not reasonably provide enablement for a method for treating a patient suffering from a cancerous disease or for a process for mediating cytotoxicity of a human tumor cell with a monoclonal antibody having the identifying characteristics of a monoclonal antibody encoded by the cloned deposited with the ATCC as PTA-4890, wherein said antibody is a **murine** antibody. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims read on treating a human cancer patient with a mouse monoclonal antibody PTA-4890. This means the claims read on, and the specification contemplates, the treatment of cancer in humans with antibodies produced in a mouse.

The specification teaches that the monoclonal antibody PTA-5643 was obtained following immunization of mice with cells from a patient's breast tumor biopsy, see p. 14, lines 10-12.

One cannot extrapolate the teachings of the specification to the scope of the claims because Winter et al (TIPS, 1993, 14:139-143) specifically teach that a major problem with the use of murine monoclonal antibodies in the treatment of human subjects is the development of human antimouse antibodies (HAMA) that can inactivate the injected antibodies. Thus, it would

be expected that the injection of cross species antibody would result in anti-other species antibodies and/or cytotoxic T cells against the injected antibody. Further, Baselga et al (J. Clin. Oncol, 1996, 14:737-744) specifically teach that murine antibodies are limited clinically because they are immunogenic.

Given the above, it is clear that it is not possible to predict that a mouse monoclonal antibody PTA-4890 would successfully treat a human tumor in a human as contemplated in the specification. Thus it would require undue experimentation to practice the broadly claimed invention.

22. Claims 1-5, 11 and 23-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-5, 11 and 23-28 are broadly drawn to a method for treating a patient suffering from a cancerous of a disease or to a process for mediating cytotoxicity of a human tumor cell with a monoclonal antibody or antigen binding fragment **having the identifying characteristics** monoclonal antibody encoded by the cloned deposited with the ATCC as PTA-4890. It is noted that although the specification teaches that PTA-4890 binds to CD63, it does not define in the specification what the identifying characteristics of PTA-4890 are. Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant

claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc.,

296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics.... i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

Thus, the instant specification may provide an adequate written description of the antibody with identifying characteristics of PTA-4890 useful for treating a patient suffering from a cancerous disease or mediating cytotoxicity of a human tumor cell per Lilly by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus". Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not describe antibodies with identifying characteristics of PTA-4890 useful for treating a patient suffering from a cancerous disease or mediating cytotoxicity of a human tumor cell in a manner that satisfies either the Lilly or Enzo standards.

The specification does not provide the complete structure of the identifying characteristics of the claimed antibody, nor does the specification provide any partial structure of such identifying characteristics, nor any physical or chemical characteristics of the said identifying characteristics nor any functional characteristics coupled with a known or disclosed correlation between structure and function. Although the specification discloses that one of the PTA-4890 antigens is CD63, the binding of CD63 by PTA-4890 does not appear to be sufficient for the cytotoxic function of PTA-4890. Thus this does not provide a description of the identifying characteristics of the claimed antibody.

The specification also fails to describe the identifying characteristics by the test set out in Lilly. Although the specification discloses that the PTA-4890 antigen is CD63, the binding of CD63 by PTA-4890 does not appear to be sufficient for the cytotoxic function of PTA-4890. Therefore, it necessarily fails to describe a "representative number" of species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Thus, the specification does not provide an adequate written description of the claimed identifying characteristics of the monoclonal antibody PTA-4890 that are required to practice the claimed invention. Since the specification fails to adequately describe the identifying characteristics of the claimed antibodies useful for treating a patient suffering from a cancerous disease or mediating cytotoxicity of a human tumor cell, it also fails to adequately describe the claimed methods.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi* , 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

23. Claim 1-5, 12-16, and 23-28 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10-12 and 14-16 of U.S. Patent No. 7,009,040 in view of Kimball (Introduction to Immunology, 3rd ed. Macmillan, Inc, New York, 1990, p. 507), and in further view of Miller and Tannock (The Basic Science of Oncology, 2nd ed., McGraw- Hill Inc., 1992, Ch.14).

Although the conflicting claims are not identical, they are not patentably distinct from each other because they relate to the same inventive concept. The instant claims are generic to the claims of the copending application and would have been obvious in view of the copending claims.

Claims 10-12 and 14-16 of US Patent No. 7,009,040 are drawn to 10) A method of treating human breast and prostate tumors susceptible to antibody induced cellular cytotoxicity in a mammal, wherein said human breast and prostrate tumors express an antigen which specifically binds to the monoclonal antibody encoded by a clone deposited with the ATCC as accession number PTA-4890 or a cellular cytotoxicity inducing antigen binding fragment thereof, comprising administering to said mammal said monoclonal antibody or said antigen binding fragment thereof in an amount effective to induce cellular cytotoxicity and thereby reduce said mammal's tumor burden; 11) The method of claim 10 wherein said monoclonal antibody is conjugated to a cytotoxic moiety; 12) The method of claim 11 wherein said cytotoxic moiety is a radioactive isotope; 14) The method of claim 10 wherein said monoclonal antibody mediates antibody dependent cellular cytotoxicity; 15) The method of claim 10 wherein said monoclonal antibody is humanized; 16) The method of claim 10 wherein said monoclonal antibody is chimerized. "A generic claim cannot be allowed to an applicant if the prior art discloses a species falling within the claimed genus." The species in that case will anticipate the genus. In re Slayter, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960); In re Gosteli, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989).

Kimball, page 507, teaches that adjuvants are material added to an antigen to increase its immunogenicity and adjuvants help stimulate immune responses to weakly immunogenic molecules, see p. 375.

Miller and Tannock teach that the nonspecific immunostimulant levamisole can lead to increased survival alone or when combined with the chemotherapeutic drug 5-fluorouracil in cancer patients, see p. 245, right column.

It would have been *prima facia* obvious to use both the antibody of claim 10 and an immunostimulatory adjuvant in combination for treating a patient suffering from a cancerous disease in view of the importance of eliminating cancer cells. Each of these agents had been taught by the prior art to be effective in treating a patient suffering from a cancerous disease, thus the instant situation is amenable to the type of analysis set forth in In re Kerkhoven, 205 USPQ 1069 (CCPA 1980) wherein the court held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order to make a third composition that is to be used for the very same purpose since the idea of combining them flows logically from their having been individually taught in the prior art. Applying the same logic to the instant composition claimed, given the teaching of the prior art of compositions using either monoclonal antibodies with the identifying characteristics of PTA-4890 or immunostimulatory adjuvants in the process in treating a patient suffering from a cancerous disease, it would have been obvious to treat a patient suffering from a cancerous disease with monoclonal antibodies with the identifying characteristics of PTA-4890 in combination with immunostimulatory adjuvants because the idea of doing so would have logically followed from their having been individually taught in the prior art to be useful as

agents for the same purpose of treating a patient suffering from a cancerous disease. One of ordinary skill in the art would have reasonably expected to obtain effective treatment with either or both of these agents since both had been demonstrated in the prior art to be effective for treating a patient suffering from a cancerous disease.

Thus one of ordinary skill in the art would have had motivation and a reasonable expectation of success in making and using the claimed invention.

Given that the claims of US Patent No 7,009,040 are a species of the instantly claimed invention, they make obvious the instantly claimed invention.

24. Claims 1, 12, 23, and 27 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 5 and 6 of copending Application No. 11/321,624, in view of Kimball (Introduction to Immunology, 3rd ed. Macmillan, Inc, New York, 1990, p. 507), and in further view of Miller and Tannock (The Basic Science of Oncology, 2nd ed., McGraw- Hill Inc., 1992, Ch.14).

Although the conflicting claims are not identical, they are not patentably distinct from each other because they relate to the same inventive concept. The instant claims are generic to the claims of the copending application and would have been obvious in view of the copending claims.

The instantly claimed method is generic to claims 5 and 6 of application number 11/321,624 which are drawn to 5) a process for treating a human cancerous tumor which expresses human CD63 antigen comprising: administering to an individual suffering from said human cancer, at least one monoclonal antibody that recognizes the same epitope or epitopes as

those recognized by a monoclonal antibody produced by a hybridoma selected from the group consisting of hybridoma cell line H460-22-1 having ATCC Accession No.PTA-4622, hybridoma cell line 1A245.6 having ATCC Accession No.PTA-4889, and hybridoma cell line 7BD-33-11A having ATCC Accession No.PTA-4890; wherein binding of said epitope or epitopes is effective in reducing tumor burden and 6) a process for treating a human cancerous tumor which expresses human CD63 antigen comprising: administering to an individual suffering from said human cancer, at least one monoclonal antibody that recognizes the same epitope or epitopes as those recognized by a monoclonal antibody produced by a hybridoma selected from the group consisting of hybridoma cell line H460-22-1 having ATCC Accession No.PTA-4622, hybridoma cell line 1A245.6 having ATCC Accession No.PTA-4889, and hybridoma cell line 7BD-33-11A having ATCC Accession No.PTA-4890; in conjunction with at least one chemotherapeutic agent; wherein said administration is effective in reducing tumor burden.

Kimball and Miller and Tannock teach as set forth above.

It would have been *prima facia* obvious to use both the antibody of claim 5 and 6 and an immunostimulatory adjuvant in combination for treating a patient suffering from a cancerous disease for the reasons set forth above.

Given that the claims of copending Application No. 11/321,624 are a species of the instantly claimed invention, they make obvious the instantly claimed invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

25. Claims 1, 12, 23, and 27 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 56 and 57 of copending Application No. 11/362,452 in view of Kimball (Introduction to Immunology, 3rd ed. Macmillan, Inc, New York, 1990, p. 507), and in further view of Miller and Tannock (The Basic Science of Oncology, 2nd ed., McGraw- Hill Inc., 1992, Ch.14).

Although the conflicting claims are not identical, they are not patentably distinct from each other because they relate to the same inventive concept. The instant claims are generic to the claims of the copending application and would have been obvious in view of the copending claims.

The instantly claimed method is generic to claims 56 and 57 of application number 11/362,452 which are drawn to 56) A process for treating a human cancerous tumor which expresses human CD63 antigen comprising: administering to an individual suffering from said human cancer, at least one monoclonal antibody or ligand that recognizes the same epitope or epitopes as those recognized by the isolated monoclonal antibody produced by a hybridoma selected from the group consisting of hybridoma cell line H460-22-1 having ATCC Accession No. PTA-4622, hybridoma cell line 1 A245.6 having ATCC Accession No. PTA-4889, hybridoma cell line 7BD-33-11A having ATCC Accession No. PTA- 4890, hybridoma cell line 7BDI-60 having ATCC Accession No. PTA-4623, hybridoma cell line 7BDI-58 having IDAC Accession No. 141205-01 and hybridoma cell line AR51 A994.1 having IDAC Accession No. 141205-06; wherein binding of said epitope or epitopes is effective in reducing tumor burden and 57) A process for treating a human cancerous tumor which expresses human CD63 antigen comprising: administering to an individual suffering from said human cancer, at least one

monoclonal antibody or ligand that recognizes the same epitope or epitopes as those recognized by the isolated monoclonal antibody produced by a hybridoma selected from the group consisting of hybridoma cell line H460-22-1 having ATCC Accession No. PTA-4622, hybridoma cell line 1 A245.6 having ATCC Accession No. PTA-4889, hybridoma cell line 7BD-33-11A having ATCC Accession No. PTA- 4890, hybridoma cell line 7BDI-60 having ATCC Accession No. PTA-4623, hybridoma cell line 7BDI-58 having IDAC Accession No. 141205-01 and hybridoma cell line AR51 A994.1 having IDAC Accession No. 141205-06; in conjunction with at least one chemotherapeutic agent; wherein said administration is effective in reducing tumor burden.

Kimball and Miller and Tannock teach as set forth above.

It would have been *prima facia* obvious to use both the antibody of claims 56 and 57 and an immunostimulatory adjuvant in combination for treating a patient suffering from a cancerous disease for the reasons set forth above. Thus one of ordinary skill in the art would have had motivation and a reasonable expectation of success in making and using the claimed invention.

Given that the claims of copending Application No. 11/362,452 are a species of the instantly claimed invention, they make obvious the instantly claimed invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

26. Claims 1-5, 12-16, and 23-28 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 6-8 and 10 of copending Application No. 11/370,203 in view of Kimball (Introduction to Immunology, 3rd ed. Macmillan, Inc, New

York, 1990, p. 507), and in further view of Miller and Tannock (The Basic Science of Oncology, 2nd ed., McGraw- Hill Inc., 1992, Ch.14).

Although the conflicting claims are not identical, they are not patentably distinct from each other because they relate to the same inventive concept. The instant claims are generic to the claims of the copending application and would have been obvious in view of the copending claims.

The instantly claimed method is generic to claims 6-8 and 10 of application number 11/370,203 which are drawn to 6) A method of treating human breast and prostate tumors susceptible to antibody induced cellular cytotoxicity in a mammal, wherein said human breast and prostate tumors express an antigen which specifically binds to the isolated monoclonal antibody encoded by a clone deposited with the ATCC as accession number PTA-4890 or a cellular cytotoxicity inducing ligand thereof, comprising administering to said mammal a monoclonal antibody or cellular cytotoxicity inducing ligand in accordance with any one of claim 1 or 2 or 3, in an amount effective to induce cellular cytotoxicity and thereby reduce said mammal's tumor burden 7) The method of claim 6 wherein said monoclonal antibody or ligand is conjugated to a cytotoxic moiety; 8) The method of claim 7 wherein said cytotoxic moiety is a radioactive isotope; 10) The method of claim 6 wherein said monoclonal antibody or ligand mediates antibody dependent cellular cytotoxicity.

Kimball and Miller and Tannock teach as set forth above.

It would have been *prima facia* obvious to use both the antibodies of claims 6 and an immunostimulatory adjuvant in combination for treating a patient suffering from a cancerous

disease for the reasons set forth above. Thus one of ordinary skill in the art would have had motivation and a reasonable expectation of success in making and using the claimed invention.

Given that the claims of copending Application No. 11/370,203 are a species of the instantly claimed invention, they make obvious the instantly claimed invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

27. Claims 1, 12, 23, and 27 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 56 and 57 of copending Application No. 11/367,798 in view of Kimball (Introduction to Immunology, 3rd ed. Macmillan, Inc, New York, 1990, p. 507), and in further view of Miller and Tannock (The Basic Science of Oncology, 2nd ed., McGraw- Hill Inc., 1992, Ch.14).

Although the conflicting claims are not identical, they are not patentably distinct from each other because they relate to the same inventive concept. The instant claims are generic to the claims of the copending application and would have been obvious in view of the copending claims.

The instantly claimed method is generic to claims 56 and 57 of application number 11/367,798 which are drawn to 56) A process for treating a human cancerous tumor which expresses human CD63 antigen comprising: administering to an individual suffering from said human cancer, at least one monoclonal antibody or ligand that recognizes the same epitope or epitopes as those recognized by the isolated monoclonal antibody produced by a hybridoma selected from the group consisting of hybridoma cell line H460-22-1 having ATCC Accession

No. PTA-4622, hybridoma cell line 1 A245.6 having ATCC Accession No. PTA-4889, hybridoma cell line 7BD-33-11A having ATCC Accession No. PTA- 4890, hybridoma cell line 7BDI-60 having ATCC Accession No. PTA-4623, hybridoma cell line 7BDI-58 having IDAC Accession No. 141205-01 and hybridoma cell line AR51 A994.1 having IDAC Accession No. 141205-06; wherein binding of said epitope or epitopes is effective in reducing tumor burden and 57) A process for treating a human cancerous tumor which expresses human CD63 antigen comprising: administering to an individual suffering from said human cancer, at least one monoclonal antibody or ligand that recognizes the same epitope or epitopes as those recognized by the isolated monoclonal antibody produced by a hybridoma selected from the group consisting of hybridoma cell line H460-22-1 having ATCC Accession No. PTA-4622, hybridoma cell line 1 A245.6 having ATCC Accession No. PTA-4889, hybridoma cell line 7BD-33-11A having ATCC Accession No. PTA- 4890, hybridoma cell line 7BDI-60 having ATCC Accession No. PTA-4623, hybridoma cell line 7BDI-58 having IDAC Accession No. 141205-01 and hybridoma cell line AR51 A994.1 having IDAC Accession No. 141205-06; in conjunction with at least one chemotherapeutic agent; wherein said administration is effective in reducing tumor burden.

Kimball and Miller and Tannock et al. teach as set forth above.

It would have been *prima facia* obvious to use both the antibody of claims 56 and 57 and an immunostimulatory adjuvant in combination for treating a patient suffering from a cancerous disease for the reasons set forth above. Thus one of ordinary skill in the art would have had motivation and a reasonable expectation of success in making and using the claimed invention.

Given that the claims of copending Application No. 11/367,798 are a species of the instantly claimed invention, they make obvious the instantly claimed invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

28. Claims 1-5, 12-16, and 23-28 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 and 6-8 of copending Application No. 11/462,092 in view of Kimball (Introduction to Immunology, 3rd ed. Macmillan, Inc, New York, 1990, p. 507), and in further view of Miller and Tannock (The Basic Science of Oncology, 2nd ed., McGraw- Hill Inc., 1992, Ch.14).

Although the conflicting claims are not identical, they are not patentably distinct from each other because they relate to the same inventive concept. The instant claims are generic to the claims of the copending application and would have been obvious in view of the copending claims.

The instantly claimed method is generic to claims 2-4 and 6-8 of application number 11/462,092 which are drawn to 2) A method of treating human breast or prostate tumors in a mammal, comprising administering to said mammal an isolated monoclonal antibody or antigen binding fragment thereof which binds to the same epitope as the monoclonal antibody produced by the hybridoma deposited with the ATCC as accession number PTA-4890 , wherein said administration is in an amount effective to induce cytotoxicity and thereby reduce said mammal's tumor burden; 3) The method of claim 2 wherein said isolated monoclonal antibody or anitgen binding fragment thereof is conjugate to a cytotoxic moiety; 4) The method of claim 3

wherein said cytotoxic moiety is a radioactive isotope; 6) The method of claim 2 wherein said isolated monoclonal antibody mediates antibody dependent cellular cytotoxicity; 7) The method of claim 2 wherein said isolated monoclonal antibody mediates is a humanized antibody;8) The method of claim 2 wherein said isolated monoclonal antibody mediates is a chimeric antibody.

Kimball and Miller and Tannock teach as set forth above.

It would have been *prima facia* obvious to use both the antibody of claims 1 and an immunostimulatory adjuvant in combination for treating a patient suffering from a cancerous disease for the reasons set forth above. Thus one of ordinary skill in the art would have had motivation and a reasonable expectation of success in making and using the claimed invention.

Given that the claims of copending Application No. 11/462,092 are a species of the instantly claimed invention, they make obvious the instantly claimed invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

29. Claims 1-5, 12-16, and 23-27 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 5-10, 12-16 of copending Application No. 11/493,047 in view of Kimball (Introduction to Immunology, 3rd ed. Macmillan, Inc, New York, 1990, p. 507), and in further view of Miller and Tannock (The Basic Science of Oncology, 2nd ed., McGraw- Hill Inc., 1992, Ch.14).

Although the conflicting claims are not identical, they are not patentably distinct from each other because they relate to the same inventive concept. The instant claims are generic to

the claims of the copending application and would have been obvious in view of the copending claims.

The instantly claimed method is generic to claims 1-4 and 6-8 of application number 11/493,047 which are drawn to 1) A method of treating primary human tumor sites and metastatic sites, wherein said primary human tumor or metastasis expresses at least one epitope of an antigen which specifically binds to the isolated monoclonal antibody produced by a clone deposited with the ATCC as accession number PTA-4890 or a CDMAB thereof, which is characterized by an ability to competitively inhibit binding of said isolated monoclonal antibody or CDMAB thereof to its target antigen, comprising administering to said mammal said isolated monoclonal antibody or said CDMAB thereof in an amount effective to result in a reduction of said mammal's tumor burden; 2) The method of claim 1 wherein said isolated monoclonal antibody or CDMAB thereof is conjugated to a cytotoxic moiety; 3) The method of claim 1 wherein said cytotoxic moiety is a radioactive isotope; 5) The method of claim 1 wherein said isolated monoclonal antibody or CDMAB thereof mediates antibody dependent cellular cytotoxicity; 6) The method of claim 1 wherein said isolated monoclonal antibody or CDMAB thereof is humanized; 7) The method of claim 1 wherein said isolated monoclonal antibody or CDMAB thereof is chimerized; 8) A method of treating primary human tumor sites and metastatic sites susceptible to antibody induced cellular cytotoxicity in a mammal, wherein said primary human tumor or metastasis expresses at least one epitope of an antigen which specifically binds to the isolated monoclonal antibody produced by a clone deposited with the ATCC as accession number PTA-4890 or a CDMAB thereof, which is characterized by an ability to competitively inhibit binding of said isolated monoclonal antibody or CDMAB thereof

to its target antigen, comprising administering to said mammal said isolated monoclonal antibody or said CDMAB thereof in an amount effective to result in a reduction of said mammal's tumor burden; 9) The method of claim 8 wherein said isolated monoclonal antibody or CDMAB thereof is conjugated to a cytotoxic moiety; 10) The method of claim 8 wherein said cytotoxic moiety is a radioactive isotope; 12) The method of claim 8 wherein said isolated monoclonal antibody or CDMAB thereof mediates antibody dependent cellular cytotoxicity; 13) The method of claim 8 wherein said isolated monoclonal antibody or CDMAB thereof is humanized; 14) The method of claim 8 wherein said isolated monoclonal antibody or CDMAB thereof is chimerized; 15) A process for treating human cancerous tumors which express an epitope or epitopes of human CD63 antigen which is specifically bound by the isolated monoclonal antibody produced by hybridoma cell line 7BD-33-11A having ATCC Accession No. PTA-4890, comprising: administering to an individual suffering from said human cancer, at least one isolated monoclonal antibody or CDMAB thereof that recognizes the same epitope or epitopes as those recognized by the isolated monoclonal antibody produced by hybridoma cell line 7BD-33-11A having ATCC Accession No. PTA-4890; wherein binding of said epitope or epitopes results in a reduction of tumor burden; 16) A process for treating human cancerous tumors which express an epitope or epitopes of human CD63 antigen which is specifically bound by the isolated monoclonal antibody produced by hybridoma cell line 7BD-33-11A having ATCC Accession No. PTA-4890, comprising: administering to an individual suffering from said human cancer, at least one isolated monoclonal antibody or CDMAB thereof that recognizes the same epitope or epitopes as those recognized by the isolated monoclonal antibody produced by

hybridoma cell line 7BD-33-11A having ATCC Accession No. PTA-4890; wherein said administration results in a reduction of tumor burden.

Kimball and Miller and Tannock teach as set forth above.

It would have been *prima facia* obvious to use both the antibody of claims 1 and an immunostimulatory adjuvant in combination for treating a patient suffering from a cancerous disease for the reasons set forth above. Thus one of ordinary skill in the art would have had motivation and a reasonable expectation of success in making and using the claimed invention.

Given that the claims of copending Application No. 11/493,047 are a species of the instantly claimed invention, they make obvious the instantly claimed invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

30. No claims are allowed.

31. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

Peter J. Reddig, Ph.D.

Examiner
Art Unit 1642

PJR